<Pymol Refresher>

Target: *T cruzi* dihydrofolate reductase-thymidilate synthase (tcDHFR-TS)

1. **2H2Q**

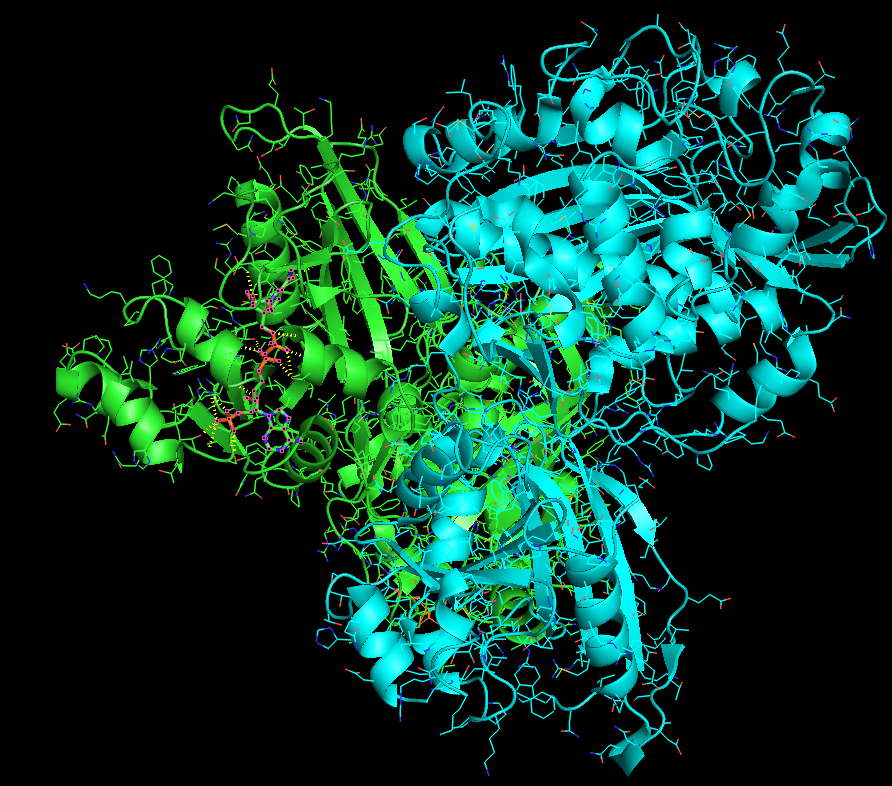


Figure 1-1. individual components of chain

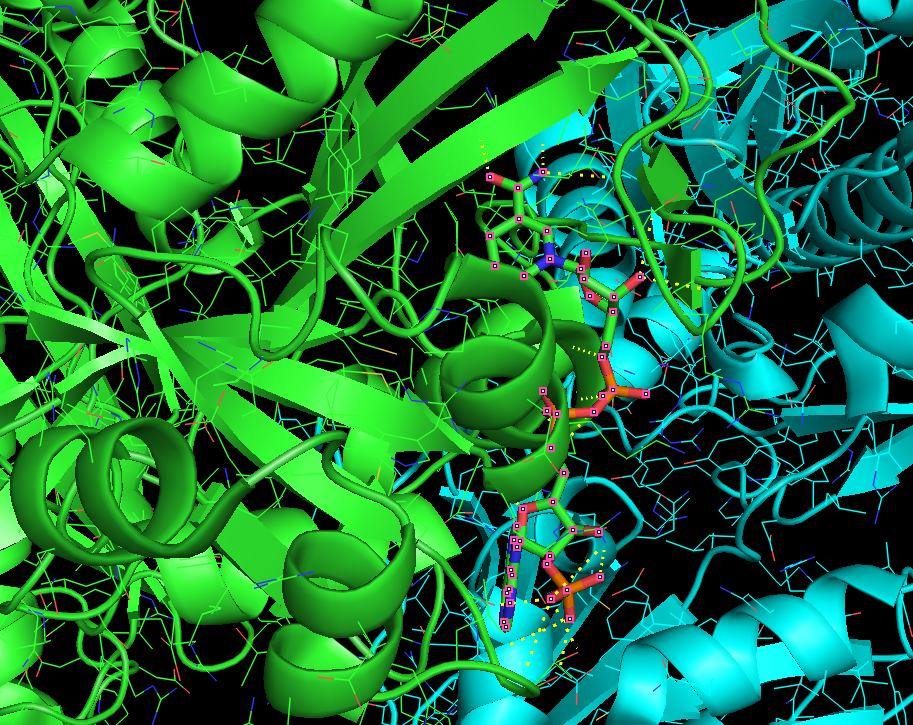


Figure 1-2. Polar contacts between protein and substrate, NAP in pink.

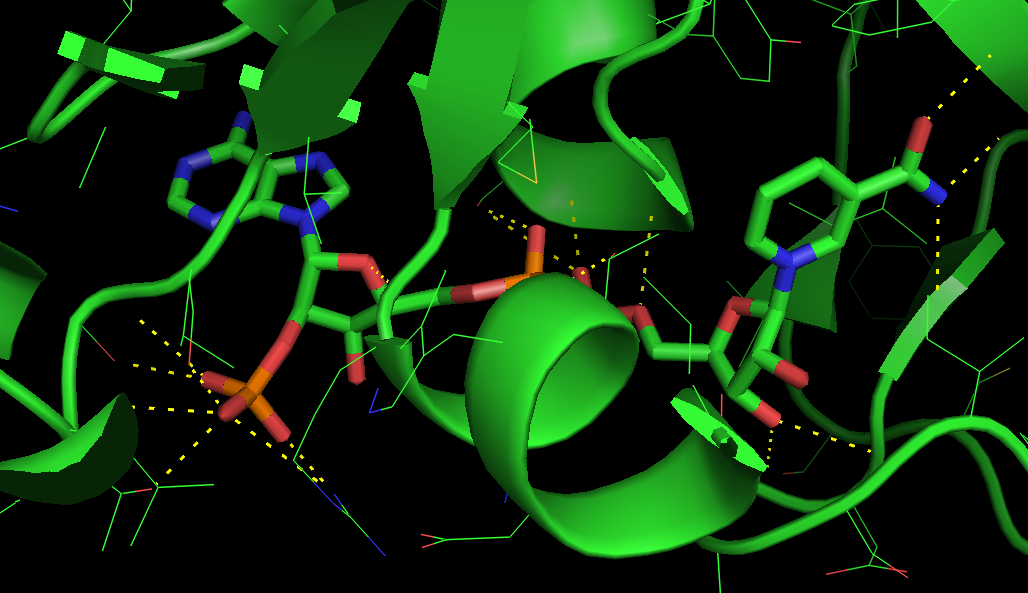


Figure 1-3. Polar contacts between protein and substrates in yellow dash line



Figure 1-4. Hydrophobic residue in yellow, Ionic residues in Blue, and Polar residues in light blue

1. **3CL9**

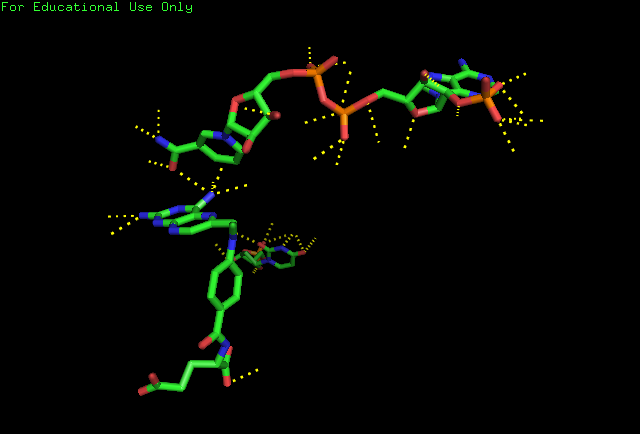


Figure 2-1. All components separately

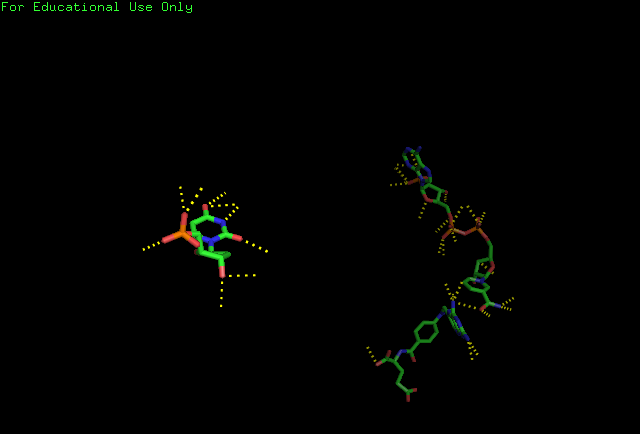


Figure 2-2. Polar contacts between the protein and polar contacts between the inhibitor(MTX) and protein.

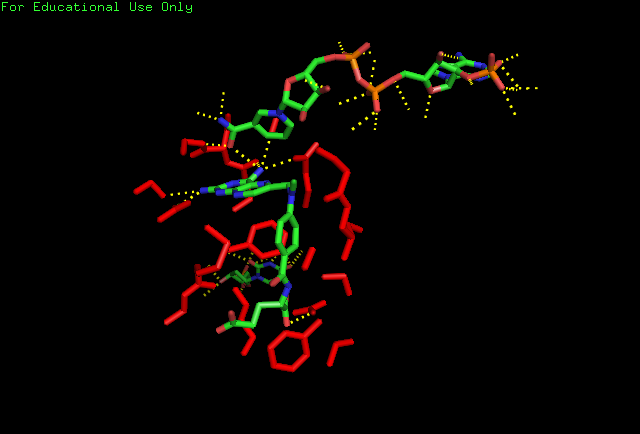


Figure 2-3. Active site around 5A(angstroms) from ligand

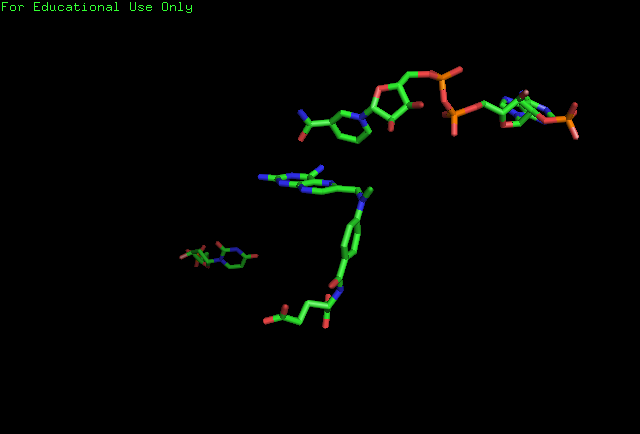


Figure 2-4. Substrates and cofactors in different color

1. **1U72**

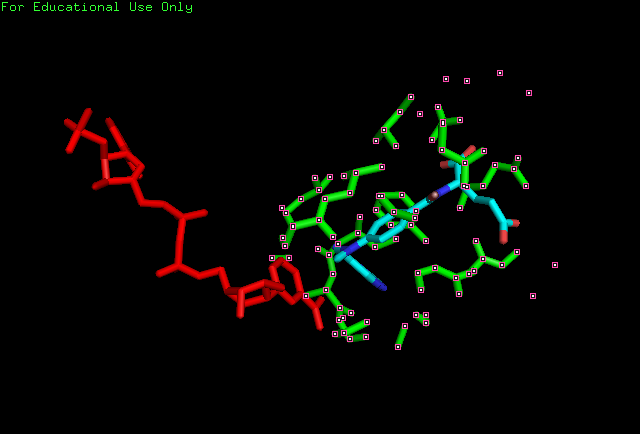


Figure 3-1. Active site around 5A(angstroms) from ligand in different colors

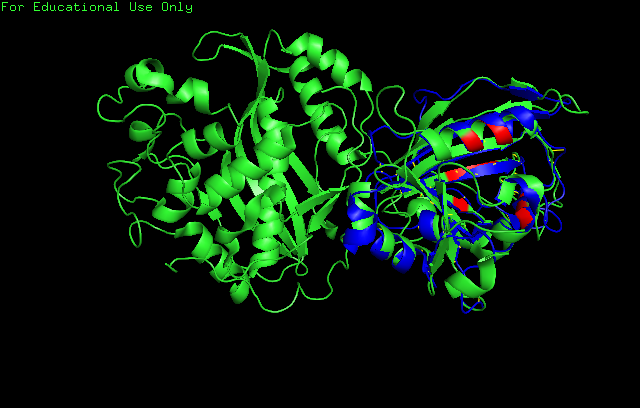
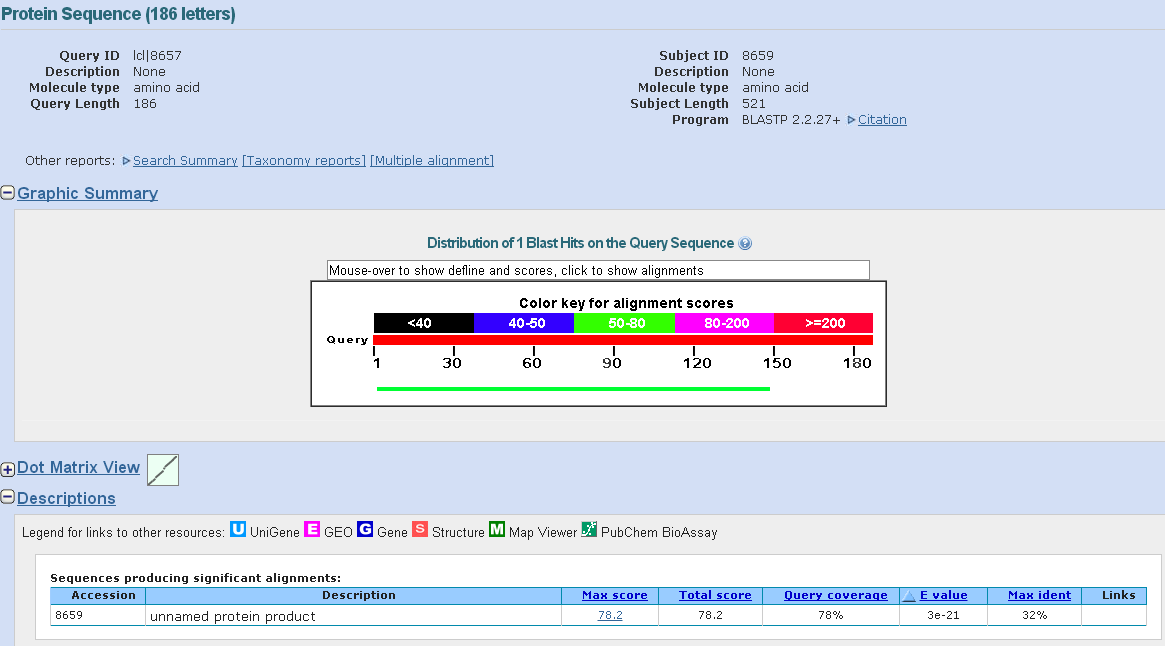


Figure 3-2. Aligned 1U72(blue) and 3CL9(green and red)

* RMS = 1.126
* The binding modes of MTX to each of these two enzymes are very close.
* The enzymes could differentially targeted with a single drug, since they have very similar MTX.
* There are differences in the amino acid sequence in the active site.
* BLAST Result:



Alignment result:



* They are not quite similar and this is a good result since it won’t inhibit human amino acid sequences.
* They have similar MTX. However, they have different amino sequences in active sites.

1U72: IVADLREFRFQTSIPNLKRVYT

3CL9: VVAIDMKFRTTSIPFLPRIGYT

1. **3HBB**

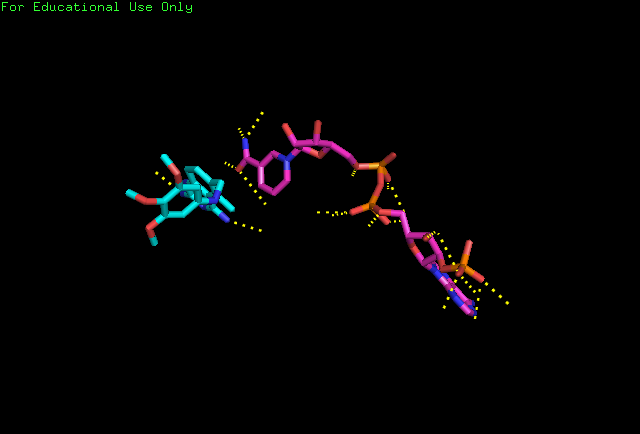


Figure 4-1. All components and polar contacts between the protein and inhibitor(TMQ)

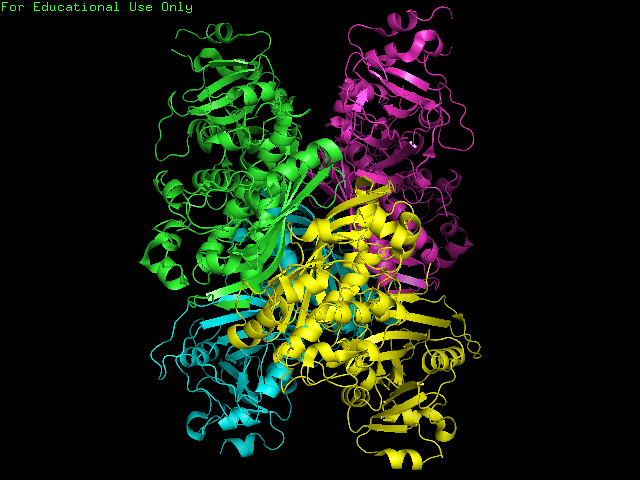


Figure 4-2. Each chain distinctively in different colors. There are four different chains.

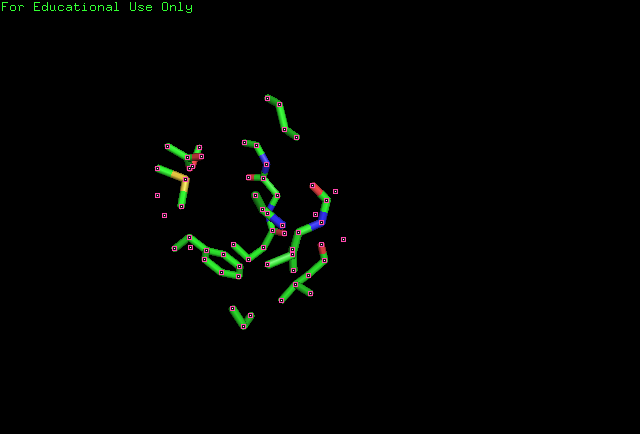


Figure 4-3. Active site around 5A(angstroms) from ligand in different colors

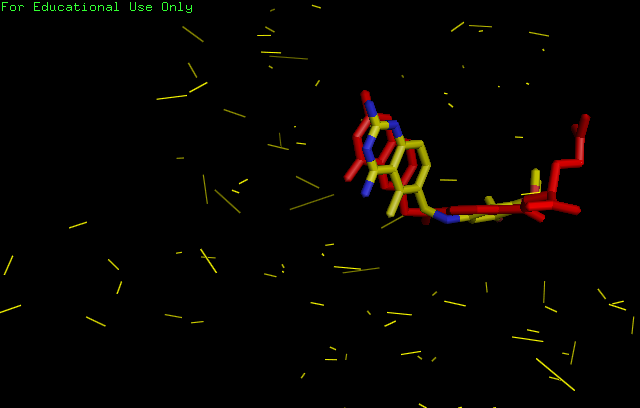
* No. Binding mode of TMQ to T. cruzi DHFR-TS not significantly different from that of MTX to human DHFR from 1U72. Because, two binding modes are similar to one active site in 3HBB. Other three active sites don’t have similar active sites in TMQ.
* 

Figure 4-4. Binding mode of TMQ to T.cruzi DHFR-TS and MTX to human DHFR from 1U72